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Professor Joshua Lederberg
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The University of Wisconsin
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Madison 6, Wisconsin

Dear Professor Lederberg,

I was glad to hear from you again. It had been my intention to send you a note about our genetics work but I never got around to it. Your surmise that the article in Heredity had excaped my notice was fully justified. Indeed, I have not read it yet and I will have to defer an extensive comment until I have done so. However, two points occur to me on reading the derivation given in your letter.

First, Neurospora conidiospores are multinucleate and one might suspect that a spore would remain viable as long as a single nucleus had survived the treatment whereas the appropriate mutation in a single nucleus would lead to a counted mutant. It has been shown, for example, by Westergaard et al in the latest issue of Hereditas and in our own work, that the mutant colonies are heterocaryotic for the reversion to wild type. This problem is further complicated by the fact that mutations preventing the independent survival of a nucleus may be compensated in some measure by the presence of nuclei not affected in the same way. Accordingly, I am not sure that a 63% mortality should be expected to give the greatest number of mutants although I would certainly like to think so.

Secondly, we have been concerned with an idea that is more or less of an obvious corollary to the one that you mention. If it is assumed that all mutations arise through the same mechanism and that the powerful mutagens kill only by the induction of lethal mutations, then all such mutagens should lead to the same maximum mutation rate based on the number of treated individuals. Our most recent data suggest that a number of chemical agents produce the same mutation rate under optimum conditions but ultra violet light clearly produces a rate about three times higher. I have tried, vainly so far, to relate this discrepancy to the fact that there are several nuclei per spore. If you have any ideas about this problem we should certainly like to hear them.

Finally, I would point out that all of this stuff breaks down if it develops that genes do not show the same relative response to different agents. We have been collecting unstable, biochemically deficient Neurospora strains and are just starting to measure their back-mutation rates after various treatments. This work is only barely under way but we have been astonished to find in our preliminary experiments evidence that the relative /potencies of different mutagenic agents are not the same when they are applied to different genes.

I also am still hoping that you can find time to repeat the specific adsorption experiments. If you do get a chance to try it , though, it would be a good idea to write for the latest receipt since some progress is being made in improving the techniques.

Regarding water elution of the gels there is no experimental evidence to show that this would be harmful. I have always used methanol. Obviously,

though, water might accelerate a deterioration of specific configurations of the surff ace. Moreover, if water were to be used as the eluent it is likely that a special technique would be required. I am working on a paper (for presentation at the Houston ACS meeting) that will contain some information that it would be important to take into account before applying these procedures to lactose. I will send a digest of this material as soon as it is in reasonable order.

All of my completed experiments have employed a simple Soxhlet extractor for removing dye from the gels. However, there is reason to believe that the gels lose their properties with aging and hence it is possible that cold extraction would give much better results. Samples prepared by extraction with cold methanol in a column have just been finished and their characteristics will be determined in the next week or so.

The study of the catalytic action of specific adsorbents is still entirely inconclusive. Gels have been prepared that were intended to simulate the action of invertase, catalase, and carbonic anhydrase but no definite results have been obtained. The first named, simply a gel prepared in the presence of sucrose, showed a spectacular positive result but a careful analysis of the experiments shows that the controls were inadequate and the work will have to be repeated.

I will have more to say about all of these things a few weeks hence.

Sincerely yours,

Frank H. Dickey

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